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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/945,166	08/31/2001	David R. Elmaleh	MGA-003.01	1584
25181	7590	12/10/2004	EXAMINER	
FOLEY HOAG, LLP PATENT GROUP, WORLD TRADE CENTER WEST 155 SEAPORT BLVD BOSTON, MA 02110			VIVLEMORE, TRACY ANN	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 12/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/945,166

**Applicant(s)**

ELMALEH ET AL.

**Examiner**

Tracy Vivlemore

**Art Unit**

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 23 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-14 and 25-34 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 8-14 and 30-34 is/are rejected.
- 7) ☒ Claim(s) 4-7 and 25-29 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>10/04</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 9, 2004 has been entered.

#### ***Claim Objections***

Claims 2 and 9 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 1 and 8 have been amended to exclude embodiments wherein a lipid is present. Claims 2 and 9 are dependent from 1 and 8, respectively and do not further limit the parent claims as they explicitly recite that the targeting moiety may be a lipid.

Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper

Art Unit: 1635

dependent form, or rewrite the claim(s) in independent form. Claim 1 has been amended to limit the claimed constructs to those that are not photoreactive. Claim 3 is dependent from 1 and does not further limit the parent claim as it explicitly recites detectable labels that are photoreactive.

***Claim Rejections - 35 USC § 112***

Applicant's amendments have overcome the rejections of record of claims 5-7, 12-14, 27 and 32 under 35 USC 112, second paragraph.

***New Claim Rejections - 35 USC § 112***

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 has been amended to insert the limitation "non-photoreactive" into the preamble. It is unknown what this limitation is referring to as claim 3 explicitly recites fluorescent labels, which are photoreactive. Additionally, claim 1 has been further amended to insert the limitation "wherein said construct does not comprise a receptor-binding internalized ligand". It is unknown what this limitation is referring to as there is no definition of this phrase anywhere in the specification. The only definition of this phrase appears in the prior art patent 6,037,329 previously used to reject these claims under 35 USC 102(b). Using the definition of "receptor-binding internalized ligand" found in the '329 patent (recited in paragraph 1 below), renders claim 1 indefinite as all the targeting moieties recited in claim 2 are receptor-binding internalized ligands.

Claims 4-7 are indefinite because they depend from claim 1.

Claim 8 recites the limitation "said construct" in lines 4 and 5. There is insufficient antecedent basis for this limitation in the claim.

Claims 9-14 recite the preamble "a...construct as in claim 8". Claim 8 is claimed as a conjugate, not a construct, therefore providing no antecedent basis for the preamble in these claims. Claims 30-34 are rejected for the same reason as they are dependent upon claim 11.

Claims 12-14 recite the limitation "said label" in lines 3-4. There is insufficient antecedent basis for this limitation in these claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 and 25-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

1. In response to a rejection under 102(b) as being anticipated by Baird et al. (US 6,037,329), claims 1 and 8 have been amended to add a limitation stating that the claimed construct does not comprise a receptor-binding internalized ligand. At column 8, lines 7-18, Baird et al. define the phrase "receptor-binding internalized ligand" as follows:

Art Unit: 1635

As used herein, "receptor-binding internalized ligand" or "ligand" refers to any peptide, polypeptide, protein or non-protein, such as a peptidomimetic, that is capable of binding to a cell-surface molecule and is internalized. Within the context of this invention, the receptor-binding internalized ligand is conjugated to a nucleic acid binding domain, either as a fusion protein or through chemical conjugation, and is used to deliver a cytocide-encoding or pro-drug encoding agent to a cell. In one aspect, the ligand is directly conjugated to a nucleic acid molecule, which may be further complexed with a nucleic acid binding domain. Such ligands include growth factors, cytokines, antibodies, hormones, and the like.

2. From this definition, it is clear that Baird et al. mean a "receptor binding internalized ligand" to be a moiety which enters a cell by binding to a cell-surface molecule that facilitate its entry into a cell. This definition encompasses the process commonly referred to in the art as receptor mediated endocytosis and also includes any other process that might allow entry into a cell such as binding to antigens or haptens.

3. Applicant's specification contemplates on page 5 that the targeting moieties of the claimed invention enter a cell: "The targeting moiety may be any molecular structure which assists the construct in localizing to a particular target area, entering a target cell(s), and/or binding to a target receptor" and "Preferred complexes are sufficiently stable to prevent significant uncoupling prior to internalization by the target cell." The specification also states entry to a cell is accomplished by a receptor-mediated endocytosis mechanism. For example, see the definition of folate on pages 6-7 and on pages 10-17, the detailed description of targeting moieties.

4. The newly added limitation specifically excludes all contemplated embodiments of the invention. The working examples provided in the specification are designed and shown to enter cells. The specification provides no guidance on how to make or use targeted oligonucleotide constructs that do not enter a cell or how to make or use targeted oligonucleotide constructs that enter a cell without binding to a receptor. Thus,

Art Unit: 1635

the specification is not enabling as it does not provide the guidance necessary for one of skill in the art to make or use the invention as claimed.

***Claim Rejections - 35 USC § 102***

Applicant's amendments have overcome the rejection of record of claims 1-14 and 25-34 as being anticipated by Baird et al.

The rejection of record of claims 1-3, 5 and 8-10 under 35 USC 102 (e) as being anticipated by Papahadjopoulos et al. is maintained. Applicant's have amended claims 1 and 8 to state the claimed construct is not encapsulated in a liposome or linked to a lipid, however claims 2 and 9 are still drawn to embodiments of the invention that encompass the presence of lipids.

The rejection of record of claims 1-3 and 5-7 under 35 USC 102 (e) as being anticipated by Rothschild et al. is maintained. Applicant's have amended claim 1 to state the claimed construct is not photoreactive, however claim 3 is still drawn to embodiments of the invention that encompass targeting moieties that are photoreactive.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

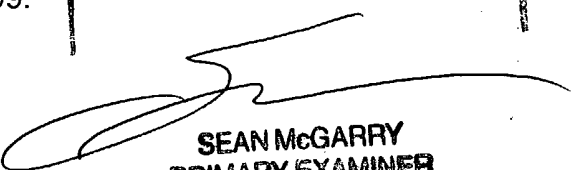
Art Unit: 1635

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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TV  
November 3, 2004

  
**SEAN McGARRY**  
**PRIMARY EXAMINER**  
1635

Tracy Vivlemore  
Examiner  
Art Unit 1635